producing a member of a specific binding pair. The examiner states that "[I]t is well known that the phage display library displays a plurality of nucleic acid sequences encoding polypeptide [sic], however, all the sequences displayed do not encode a specific binding pair member of interest (may not bind to the ligand)." Applicants traverse the rejection and request consideration.

The independent claims are directed to a "method of producing a member of a specific binding pair...." In essence, the point is that specific binding pair members are produced on the surface of filamentous bacteriophage particles by expressing encoding nucleic acid in recombinant cells. It is not a requirement for *production* of a specific binding pair member that the specific binding pair member bind to a ligand of interest as the Examiner suggests. The steps recited in, for example, claim 145, are all the steps necessary for the specific binding pair member to be produced and displayed at the surface of filamentous bacteriophage. In fact in the method of claim 145, the nucleic acid expressed in recombinant host cells which encodes a genetically diverse population of polypeptides is provided by mutating nucleic acid which is known to encode a specific binding pair member, in this case an enzyme. The addition of a requirement for a screening or selection step is onerous and overly limiting as screening or selection are optional steps that may be carried out after the specific binding pair members have been produced as specifically recited in Claim 145. Because the claim recites the necessary steps for producing the recited specific binding pair members, the Applicants respectfully submit that the rejections should be withdrawn and withdrawal is requested.

B. Rejections Under 35 USC §103(a) Should be Withdrawn

The Examiner maintained the previous rejection of claims 45-65, 78-109 and 145 under 35 USC §103(a), alleging that the claims were obvious in view of the disclosure of Dower. The Examiner alleges that it would have been obvious to a person skilled in the art

at the time the invention was made to use the general screening method taught by Dower to screen a specific binding pair member which binds an enzyme.

The Applicants respectfully traverse the rejections because Dower *et al.* fails *inter alia* to teach or suggest a method as presently claimed which includes the mutation of a starting molecule wherein the starting molecule is an enzyme which is a non-immunoglobulin protein, and further does not teach or suggest enzymes of at least 100 amino acids. While Dower does mention enzymes, such mention is not germane to the claims of this invention. Dower refers to cloning such genes from a nucleotide library – i.e., prepare a natural library then look to clone a single protein that binds a ligand that you have. Dower simply does not teach or suggest that any such enzyme molecule (or its encoding nucleic acid) may serve as starting molecules whose encoding nucleic acid is mutated to generate upon expression its host cells a genetically diverse population of polypeptides as is required by this invention.

Regarding the mutation step utilized in the practice of the applicants' invention, the Examiner's suggestion that the cloning techniques to be employed by Dower mean that it teaches "that the nucleic acid sequence would undergo mutation or recombination before it has been inserted into the vectors" lacks factual basis and further lacks a mechanistic basis by which a genetically diverse population of polypeptides could be so produced. The Examiner has failed to provide any substantiation for the contention that cloning techniques result in mutations. Contrary to the Examiner's apparent belief, recombination is not mutation. Absent such substantiation, the Applicants respectfully submit that the rejection on that basis is unsustainable. Further, Applicants reiterate that Dower simply does not teach or suggest the mutation of nucleic acid encoding a parent enzyme so as to generate a diverse population of polypeptides as called for by the claims. Because Dower *et al.* fails to

teach or suggest such elements of the present claims, the Applicants respectfully submit that the rejections should be withdrawn.

II. Conclusion

Applicants believe all the claims are in condition for allowance. Favorable consideration of the application is respectfully requested. The Examiner is invited to contact the undersigned with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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